



4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2013-D-0369]

M7(R1) Addendum to ICH M7; International Conference on Harmonisation; Draft Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance entitled “M7(R1) Addendum to ICH M7: Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk; Application of the Principles of the ICH M7 Guidance to Calculation of Compound-Specific Acceptable Intakes.” The draft guidance was prepared under the auspices of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). This draft guidance, an addendum to the ICH M7 guidance of May 28, 2015, provides guidance on acceptable intake limits derived for some chemicals that are considered to be mutagens and carcinogens, and that were selected because they are commonly used in pharmaceutical manufacturing or are useful in illustrating the principles for deriving compound-specific intakes as described in ICH M7. The draft guidance is intended to provide guidance for new drug substances and new drug products during their clinical development and subsequent applications for marketing.

DATES: Although you can comment on any guidance at any time (see 21 CFR 10.115 (g)(5)), to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance, submit either electronic or written comments on the draft guidance by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: Submit written requests for single copies of the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Hillandale Building, 4th Floor, Silver Spring, MD 20993-0002, or the Office of Communication, Outreach and Development, Center for Biologics Evaluation and Research (CBER), Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, rm. 3128, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist the office in processing your requests. The draft guidance may also be obtained by mail by calling CBER at 1-800-835-4709 or 240-402-8010. See the SUPPLEMENTARY INFORMATION section for electronic access to the draft guidance document.

Submit electronic comments on the draft guidance to <http://www.regulations.gov>.

Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Regarding the guidance: Aisar Atrakchi, Center for Drug Evaluation and Research, Food and Drug Administration, Bldg. 22, rm. 4118, Silver Spring, MD 20993-0002, 301-796-1036; or Anne Pilaro, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, rm. 4025, Silver Spring, MD 20993-0002, 240-402-8341.

Regarding the ICH: Michelle Limoli, Center for Drug Evaluation and Research, International Programs, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, rm. 7208, Silver Spring, MD 20993-0002, 301-796-8377.

SUPPLEMENTARY INFORMATION:

I. Background

In recent years, many important initiatives have been undertaken by regulatory authorities and industry associations to promote international harmonization of regulatory requirements. FDA has participated in many meetings designed to enhance harmonization and is committed to seeking scientifically based harmonized technical procedures for pharmaceutical development. One of the goals of harmonization is to identify and then reduce differences in technical requirements for drug development among regulatory agencies.

ICH was organized to provide an opportunity for tripartite harmonization initiatives to be developed with input from both regulatory and industry representatives. FDA also seeks input from consumer representatives and others. ICH is concerned with harmonization of technical requirements for the registration of pharmaceutical products among three regions: Europe, Japan, and North America. The eight ICH sponsors are the European Commission; the European Federation of Pharmaceutical Industries Associations; the Japanese Ministry of Health, Labour, and Welfare; the Japanese Pharmaceutical Manufacturers Association; CDER and CBER, FDA; the Pharmaceutical Research and Manufacturers of America; Health Canada; and Swissmedic. The ICH Secretariat, which coordinates the preparation of documentation, is provided by the International Federation of Pharmaceutical Manufacturers Associations (IFPMA).

The ICH Steering Committee includes representatives from each of the ICH sponsors and the IFPMA, as well as observers from the World Health Organization.

In June 2015, the ICH Steering Committee agreed that the following draft guidance should be made available for public comment: “M7(R1) Addendum to ICH M7: Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk; Application of the Principles of the ICH M7 Guidance to Calculation of Compound-Specific Acceptable Intakes.” The draft guidance is the product of the Expert Working Group of the ICH. Comments about this draft will be considered by FDA and the Expert Working Group.

The draft guidance provides guidance on acceptable intake limits derived for some chemicals that are considered to be mutagens and carcinogens and that were selected because they are commonly used in pharmaceutical manufacturing or are useful in illustrating the principles of deriving compound-specific intakes as described in ICH M7. The default method from ICH M7 of linear extrapolation from the cancer potency estimate, TD_{50} , is used as the primary method to derive the acceptable intakes for carcinogens with likely mutagenic mode of action.

This draft guidance is being issued consistent with FDA’s good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the current thinking of FDA on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations.

II. Comments

Interested persons may submit either electronic comments regarding this document to <http://www.regulations.gov> or written comments to the Division of Dockets Management (see ADDRESSES). It is only necessary to send one set of comments. Identify comments with the

docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday, and will be posted to the docket at <http://www.regulations.gov>.

III. Electronic Access

Persons with access to the Internet may obtain the document at <http://www.regulations.gov>,
<http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>,
or
<http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>.

Dated: September 22, 2015.

Leslie Kux,

Associate Commissioner for Policy.

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